UNITED STATES PATENT APPLICATION

CARDIAC RHYTHM MANAGEMENT SYSTEM AND METHOD USING TIME BETWEEN MITRAL VALVE CLOSURE AND AORTIC EJECTION

INVENTORS

William C. Lincoln
of Coon Rapids, MN, USA

Gerrard M. Carlson
of Champlin, MN, USA

Attorney: Suneel Arora
Reg. No. 42,267
Schwegman, Lundberg, Woessner, & Kluth, P.A.
1600 TCF Tower
121 South Eighth Street
Minneapolis, Minnesota 55402

ATTORNEY DOCKET NO. 00279.424US1

CARDIAC RHYTHM MANAGEMENT SYSTEM AND METHOD USING TIME BETWEEN MITRAL VALVE CLOSURE AND AORTIC EJECTION

TECHNICAL FIELD

This document relates generally to medical systems, devices, and methods, and particularly, but not by way of limitation, to a cardiac rhythm management system using a time between a mitral valve closure and an aortic ejection, such as for prediction, diagnosis, and/or treatment.

BACKGROUND

When functioning properly, the human heart maintains its own intrinsic rhythm. Its sinoatrial node generates intrinsic electrical cardiac signals that depolarize the atria, causing atrial heart contractions. Its atrioventricular node then passes the intrinsic cardiac signal to depolarize the ventricles, causing ventricular heart contractions. These intrinsic cardiac signals can be sensed on a surface electrocardiogram (ECG) obtained from electrodes placed on the patient's skin, or from electrodes implanted within the patient's body. The surface ECG waveform, for example, includes artifacts associated with atrial depolarizations ("P-waves") and those associated with ventricular depolarizations ("QRS complexes").

A normal heart is capable of pumping adequate blood throughout the body's circulatory system. However, some people have irregular cardiac rhythms, referred to as cardiac arrhythmias. Moreover, some patients have poorly spatially-coordinated heart contractions. In either case, diminished blood circulation may result. For such patients, a cardiac rhythm management system may be used to improve the rhythm and/or spatial coordination of heart contractions. Such systems are often implanted in the patient and deliver therapy to the heart.

Cardiac rhythm management systems include, among other things, pacemakers, also referred to as pacers. Pacers deliver timed sequences of low energy electrical stimuli, called pace pulses, to the heart, such as via an intravascular

lead wire or catheter (referred to as a "lead") having one or more electrodes disposed in or about the heart. Heart contractions are initiated in response to such pace pulses (this is referred to as "capturing" the heart). By properly timing the delivery of pace pulses, the heart can be induced to contract in proper rhythm, greatly improving its efficiency as a pump. Pacers are often used to treat patients with bradyarrhythmias, that is, hearts that beat too slowly, or irregularly. Such pacers may also coordinate atrial and ventricular contractions to improve pumping efficiency.

Cardiac rhythm management systems also include cardiac resynchronization therapy (CRT) devices for coordinating the spatial nature of heart depolarizations for improving pumping efficiency. For example, a CRT device may deliver appropriately timed pace pulses to different locations of the same heart chamber to better coordinate the contraction of that heart chamber, or the CRT device may deliver appropriately timed pace pulses to different heart chambers to improve the manner in which these different heart chambers contract together.

Cardiac rhythm management systems also include defibrillators that are capable of delivering higher energy electrical stimuli to the heart. Such defibrillators include cardioverters, which synchronize the delivery of such stimuli to sensed intrinsic heart activity signals. Defibrillators are often used to treat patients with tachyarrhythmias, that is, hearts that beat too quickly. Such too-fast heart rhythms also cause diminished blood circulation because the heart isn't allowed sufficient time to fill with blood before contracting to expel the blood. Such pumping by the heart is inefficient. A defibrillator is capable of delivering a high energy electrical stimulus that is sometimes referred to as a defibrillation countershock, also referred to simply as a "shock." The countershock interrupts the tachyarrhythmia, allowing the heart to reestablish a normal rhythm for the efficient pumping of blood. In addition to pacers, CRT devices, and defibrillators, cardiac rhythm management systems also include devices that combine these functions, as well as monitors, drug delivery devices, and any other implantable or external

systems or devices for diagnosing or treating the heart.

One problem presented by some cardiac patients is predicting which patients will likely benefit from cardiac resynchronization therapy (e.g., left ventricular pacing, bi-ventricular pacing, and/or multisite pacing within the same heart chamber). Needlessly applying CRT pacing pulses in a patient that will not benefit from such therapy may waste energy, reducing the longevity of an implanted CRM device. Moreover, delivering CRT therapy may involve implanting additional electrodes, which may increase a patient's cost and risks. Another problem presented by some cardiac patients is determining which patients are actually benefitting from the CRT or other therapy that they are receiving. Yet another problem presented by some cardiac patients is determining whether a particular CRT or other therapy benefits a particular patient more or less than another different CRT or other therapy. For these and other reasons, the present inventors have recognized that there exists an unmet need for a predictor and/or indicator of patient wellness and/or the efficacy of CRT or other therapy.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, which are offered by way of example, and not by way of limitation, and which are not necessarily drawn to scale, like numerals describe substantially similar components throughout the several views. Like numerals having different letter suffixes represent different instances of substantially similar components.

Figure **1** is a schematic/block diagram illustrating generally one example of portions of the present cardiac rhythm management system and an environment in which it is used.

Figure **2** is a schematic/block diagram illustrating generally one example of portions of an MVC detector.

Figure **3** is a flow chart illustrating generally one example of a technique for

determining whether a particular subject will likely respond to CRT.

Figure **4** is a graph of patient data illustrating generally one example of MVC-to-AE intervals versus Atrial - Ventricular Interval ("AVI").

Figure **5** is a block diagram illustrating generally one example of how the value of the MVC-to-AE interval is used as a wellness and/or therapy efficacy indicator, and/or to adjust therapy to increase efficacy and/or wellness.

SUMMARY

This document discusses, among other things, cardiac rhythm management systems and methods using the MVC-to-AE time between mitral valve closure ("MVC") and aortic ejection ("AE") of the same heart contraction, sometimes referred to as the isovolumic contraction time ("ICVT"). In one example, the MVC-to-AE time is used for predicting which patients will respond to cardiac resynchronization therapy (CRT), or other therapy. In another example, the MVC-to-AE time is used as a wellness indicator. In a further example, the MVC-to-AE time is used to select or control a therapy or therapy parameter. In one example, the MVC and AE are obtained using an accelerometer signal, however, plethysmography, tonometry, or other techniques may alternatively be used.

In one example, this document discusses, among other things, a system including an accelerometer, a mitral valve closure (MVC) detector circuit, an aortic ejection detector circuit, a timer, and a classification module. The accelerometer is configured to detect an acceleration signal in a subject. The MVC detector circuit is coupled to the accelerometer to receive the acceleration signal. The MVC detector circuit is configured to detect an MVC indication using information from the acceleration signal. The AE detector circuit is configured to detect an AE indication. The timer is coupled to the MVC detector circuit and the AE detector circuit. The timer is configured to measure a time interval between the MVC indication and the AE indication. The classification module is coupled to the timer

to receive the measured time interval. The classification module is configured to classify the subject based on the measured time interval.

In another example, this document discusses, among other things, a method including detecting in a subject an accelerometer-based mitral valve closure (MVC) indication, detecting an aortic ejection (AE) indication, measuring a time interval between the MVC indication and the AE indication, and classifying the subject based on the measured time interval.

In another example, this document discusses, among other things, a system including an accelerometer, an MVC detector circuit, an AE detector circuit, a timer, and a wellness indicator module. The accelerometer is configured to detect an acceleration signal in a subject. The MVC detector circuit is coupled to the accelerometer to receive the acceleration signal, and is configured to detect an MVC indication using information from the acceleration signal. The AE detector circuit is configured to detect an AE indication. The timer is coupled to the MVC detector circuit and the AE detector circuit. The timer is configured to measure a time interval between the MVC indication and the AE indication. The wellness indicator module is coupled to the timer to receive the measured time interval, and is configured to compute a wellness indication of the subject based on the measured time interval.

In another example, this document discusses, among other things, a method including detecting in a subject an accelerometer-based mitral valve closure (MVC) indication, detecting an aortic ejection (AE) indication, measuring a time interval between the MVC indication and the AE indication, and computing a wellness indication of the subject based on the measured time interval. Other aspects of the discussed systems, methods, and apparatuses will become apparent upon reading the following detailed description and viewing the drawings that form a part thereof.

DETAILED DESCRIPTION

In the following detailed description, reference is made to the accompanying drawings which form a part hereof, and in which is shown by way of illustration specific embodiments in which the invention may be practiced. These embodiments are described in sufficient detail to enable those skilled in the art to practice the invention, and it is to be understood that the embodiments may be combined, or that other embodiments may be utilized and that structural, logical and electrical changes may be made without departing from the spirit and scope of the present invention. The following detailed description is, therefore, not to be taken in a limiting sense, and the scope of the present invention is defined by the appended claims and their equivalents.

This document discusses systems and methods using a time interval from mitral valve closure to aortic ejection. These systems and methods will be described in applications involving implantable medical devices including, but not limited to, implantable cardiac rhythm management systems such as pacemakers, cardioverter/defibrillators, pacer/defibrillators, biventricular or other multi-site resynchronization or coordination devices, and drug delivery systems. However, these systems and methods may be employed in unimplanted devices, including, but not limited to, external pacemakers, cardioverter/defibrillators, pacer/defibrillators, biventricular or other multi-site resynchronization or coordination devices, monitors, programmers and recorders, whether such devices are used for providing a diagnostic, a therapy, or both a diagnostic and a therapy.

Figure **1** is a schematic/block diagram illustrating generally one example of portions of the present cardiac rhythm management system **100** and an environment in which it is used. In this example, system **100** includes, among other things, cardiac rhythm management device **105**, which is coupled by leads **110A-B** to heart **115**. In this illustrative example, lead **110A** is introduced into a right atrium, lead **110B** is introduced into the right ventricle, and lead **700** is introduced through

coronary sinus **702** such that electrodes **704** and **706** are communicatively coupled to a left ventricle portion of heart **115**.

In one example device **105** also includes an accelerometer **170**, such as within the housing of device **105**, which is pectorally or abdominally implanted close enough to heart **115** to sense acceleration from heart contractions. Accelerometer **170** outputs a heart acceleration signal to analog-to-digital ("A/D") converter **175**, for conversion into a digitized signal. A/D converter is coupled to controller **180** to provide the digitized acceleration signal to controller **180**.

Controller **180** is capable of sequencing through various control states such as, for example, by using a digital microprocessor having executable instructions stored in an associated instruction memory circuit, a microsequencer, or a state machine. In operation, by execution of these instructions, controller **180** implements a mitral valve closure ("MVC") detector circuit **182**, a timer **184**, a memory **186**, and an aortic ejection ("AE") detection circuit **188**. In one example, MVC detector **182** is coupled to accelerometer **170** through A/D converter **175** such that it receives the digitized heart acceleration signal. Using this digitized heart acceleration signal, MVC detector **182** detects mitral valve closure of heart **115.** The corresponding time of this event is input to timer **184**. In one example, AE detector **188** is coupled to accelerometer **170** through A/D converter **175** such that it receives the digitized heart acceleration signal. Using this digitized heart acceleration signal, AE detector **188** detects aortic ejection of blood flow. The corresponding time of this event is input to timer **184**.

Timer **184** measures the time of MVC to the later time of the corresponding AE of the same heart contraction. This time is referred to as the MVC-to-AE interval and is sometimes called the isovolumic contraction time ("IVCT") interval. Classification module **190** is coupled to the timer **184** and receives the measured MVC-to-AE interval. In one example, the classification module **190** includes a comparator that compares the measured MVC-to-AE interval against a

predetermined interval or range of intervals, such as a a normal or control range of intervals, to predict whether or how the subject will respond to CRT. In one example, the subject is deemed a likely responder to CRT if the MVC-to-AE interval exceeds a predetermined threshold value. In this example the threshold is selected between about 50 milliseconds and about 80 milliseconds, such as about 78 milliseconds, by way of example, but not by way of limitation. In another example, the classification module **190** includes a difference circuit. One input of the difference circuit receives a predetermined threshold value for the MVC-to-AE interval. The second input to the difference circuit receives the measured MVC-to-AE interval. The difference circuit subtracts the predetermined threshold from the measured MVC-to-AE interval to output an indication of a degree to which the subject is likely to respond to CRT. In a further example, the measured MVC-to-AE interval, or an indication of whether the threshold value was exceeded, is provided to transceiver **192**, which is coupled to controller **180**, and transmitted to external interface **194**, such as for display to a physician or other user, such as on a computer monitor, printout, or other data output mechanism.

Figure **2** is a schematic/block diagram illustrating generally one example of portions of MVC detector **182**. In this example, MVC detector **182** includes a highpass filter **200**, a lowpass filter **202**, a highpass filter **205**, and a peak detector **210**, although it is understood that certain of these components could be combined rather than implemented separately (e.g., a highpass and lowpass filter could be combined into a bandpass filter, etc.). In one example, highpass filter **200** receives the digitized heart acceleration signal from A/D converter **175**, removes baseline (i.e., constant or low frequency drift) signal components, and provides a resulting output signal to an input of lowpass filter **202**. In this example, lowpass filter **202** is a 5-sample moving average "boxcar" filter attenuating signal frequencies above approximately 100 Hz. Lowpass filter **202** receives the baseline-filtered heart acceleration signal from highpass filter **200**, and outputs a resulting lowpass filtered

heart acceleration signal to an input of highpass filter **205**. In one example, highpass filter **205** is a differentiator that takes a first derivative of its input lowpass filtered heart acceleration signal, received from the output of lowpass filter **202**, and outputs a resulting first derivative heart acceleration signal to an input of peak detector **210**. In one example, peak detector **210** detects negative peaks of the first derivative heart acceleration signal. However, it is understood that a polarity reversal of accelerometer **170** and/or signal inversion(s) in the signal processing path of the heart acceleration signal may alternatively use a detection of positive peaks of the first derivative heart acceleration signal. For each cycle of heart contraction and heart relaxation ("cardiac cycle"), the first negative peak of the first derivative heart acceleration signal occurring after an intrinsic or paced ventricular depolarization and before the next intrinsic or paced atrial depolarization is deemed an MVC fiducial point associated with the mitral valve closure. An indication of the time at which such MVC fiducial points occur is provided by MVC detector **182** to timer **184** for calculation of the corresponding MVC-to-AE time interval discussed above.

In one example, AE detector **188**, includes a matched filter to detect the AE from the digitized acceleration signal. One example of a matched filter is described in Carlson U.S. Patent No. 5,674,256, CARDIAC PRE-EJECTION PERIOD DETECTION, which is assigned to Cardiac Pacemakers, Inc., and which is incorporated by reference herein in its entirety, including its description of a matched filter. In this example, a predetermined model accelerometer signal, including AE fiducial information, evaluated during baseline conditions is obtained from a patient or population. The model signal segment is used as a template during an auto-regression ("AR") comparison. In one example, the segment's starting and ending points are defined with respect to ECG fiducial points and/or accelerometer fiducial points such as MVC. The AR compares the accelerometer signal obtained from the subject to the AE fiducial information of the model signal segment. The AR yields a statistical figure of merit that is evaluated to provide the AE time.

Figure **3** is a flow chart illustrating generally one example of a technique for determining whether a particular subject will likely respond to CRT (i.e., subject is deemed a likely responder). At **300,** the accelerometer signal is received. At **305**, the baseline dc or low frequency component of the acceleration signal is removed by highpass filtering. At **310**, the heart acceleration signal is lowpass filtered. At **315**, the lowpass filtered heart acceleration signal is differentiated to obtain a resulting first derivative heart acceleration signal. Then, operations are carried out for obtaining the MVC and AE times; some of these operations may be carried out substantially concurrently.

At **320**, the time of a fiducial associated with an intrinsic or paced ventricular depolarization is determined. At **325**, a first positive or negative peak of the first derivative heart acceleration signal (i.e., in this case, a first negative peak occurring after the intrinsic or paced ventricular depolarization and before a next intrinsic or paced atrial depolarization) is detected and deemed a fiducial point associated with mitral valve closure for that cardiac cycle. At **330**, the MVC time is noted. In this example, at **335**, the aortic ejection (AE) time is determined by auto-regression matching of a segment of the accelerometer signal (occurring after the R-wave fiducial is detected at **320**) to a predetermined model or template, such as by using the matched filter technique described in Carlson (U.S. Pat. No. 5,674,256). The time of the AE is noted at **340**. At **345**, the difference between the times of the AE and MVC events is calculated, yielding an MVC-to-AE time interval. If, at **350**, the MVC-to-AE time interval exceeds the predetermined threshold value, the subject is classified as a responder at **360**. If the threshold value exceeds the MVC-to-AE time interval, the subject is classified as a non-responder at **355**. The case where the MVC-to-AE time equals the threshold value can be arbitrarily assigned to either the responder or non-responder classification. Figure **4** is a graph of patient data illustrating generally one example of MVC-to-AE intervals versus Atrial - Ventricular Interval ("AVI"). In this example, a threshold value of 60 ms was used

to effectively separate responders and non-responders. However, another threshold value may also be used, as discussed above.

In an alternate example, the MVC-to-AE time interval is used in conjunction with another indicator to classify a patient as a responder or non-responder. In one example, if a patient's MVC-to-AE interval exceeds a first predetermined threshold (e.g., 60 ms) and the patient's QRS width (i.e., the duration of the QRS complex measured from a lead electrode, or otherwise) exceeds a second predetermined threshold (e.g., 155 ms, for one example of a QRS complex obtained from surface ECG electrode; a different value may be appropriate for a QRS complex obtained from an intracardiac electrogram electrode), the patient is classified as a responder and/or further classified as a "robust" responder. In one example, the QRS width is measured from at least one cardiac signal received from at least one lead electrode, using one or more level detectors, to detect the beginning and end of the QRS complex, and a timer to measure the time difference between the measured beginning and end of the QRS complex.

Figure **5** is a block diagram illustrating generally one example of how the value of the MVC-to-AE interval is used as a contractility indicator, a wellness indicator; and/or therapy efficacy indicator, and/or to adjust therapy to increase efficacy and/or contractility or wellness. In this example, the output of a comparator or other difference circuit in the classification (and/or wellness indicator) module **190** indicates a difference between the measured MVC-to-AE interval and a threshold value. In one example, the threshold value is the threshold for responder/non-responder classification discussed above. In another example, the threshold value is an MVC-to-AE interval chosen from the normal or control range of intervals. In this example the threshold is selected between about 30 milliseconds and about 50 milliseconds, such as about 40 milliseconds, by way of example, but not by way of limitation. This indication may vary over a plurality of cardiac cycles, and is therefore used as a wellness indicator. Alternatively, the wellness indicator

may be the measured MVC-to-AE interval obtained over a plurality of cardiac cycles. The wellness indicator indicates greater wellness for a shorter measured MVC-to-AE interval than for a longer measured MVC-to-AE interval. The wellness indicator can be averaged and can also be used to indicate therapy efficacy for the cardiac rhythm management being provided. In one example, the wellness indicator is used to compare the efficacy of particular therapies (e.g. Therapy 1, Therapy 2,... Therapy N) for selecting and using a therapy that the wellness indicator deems relatively more effective. In another example, the wellness indicator is used to evaluate the efficacy of a single therapy having a variable parameter (e.g., DDD pacing with variable AV delay) so that a particular value of the therapy parameter (e.g., AV delay, pacing electrode selection, interventricular delay, etc.) can be selected to obtain a higher degree of wellness. In another example, the wellness indicator is used by a therapy selection module **400** to determine or control a specific therapy, or therapy parameter (e.g., AV delay, pacing electrode selection, interventricular delay, etc.), for the cardiac rhythm management being provided.

One example of controlling a therapy uses cardiac resynchronization therapy (CRT) delivering appropriately timed pace pulses to multiple sites in one or more heart chambers to better coordinate the spatial nature of the heart contraction. One such example couples heart chamber stimulation circuit **165** to multiple electrode lead **700** in Figure **1**. Another possible example of the therapy delivers appropriately timed pace pulses to different heart chambers to improve the manner in which these different heart chambers contract together. One such example includes multiple electrode leads **700** and **110** in Figure **1** coupled to heart chamber stimulation circuits **165** and **160**. In this example, therapy module **400** determines whether CRT is needed and determines the timing of the pulses delivered to the electrodes.

Although certain examples of the system and its operation have been described above using a signal from an implanted accelerometer to determine the

time of MVC, and an acceleration-based AR comparison to determine the time of AE, it is understood that other embodiments of the system may obtain these measurements differently. One example uses an accelerometer signal generated from an accelerometer temporarily mounted on the patient's chest to detect MVC. Another example detects AE by non-invasively monitoring the carotid arterial-pulse or by using a catheter to invasively monitor aortic pressure, such as in the ascending portion of the aorta. An example of non-invasively monitoring uses plethysmography (recording changes of the size of a part as modified by the circulation of blood in it, for example, using a finger cuff and infrared light measurement) or tonometry (measurement of tension or pressure, for example, at the carotid artery).

It is to be understood that the above description is intended to be illustrative, and not restrictive. For example, the above-discussed examples may be used in combination with each other. Many other embodiments will be apparent to those of skill in the art upon reviewing the above description. The scope of the invention should, therefore, be determined with reference to the appended claims, along with the full scope of equivalents to which such claims are entitled. In the appended claims, the terms "including" and "in which" are used as the plain-English equivalents of the respective terms "comprising" and "wherein." Moreover, the terms "first," "second," "third," etc. are used merely as labels, and are not intended to impose numeric requirements on their objects.